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Original Research Article

EXTENDED TRANSSTERNAL THYMECTOMY VERSUS CONSERVATIVE MANAGEMENT IN NON-THYMOMATOUS

G.N.Prabhu[1], M. Dharmesh Raj[2], Caroline Rachel Kumara Das[3], R. Swaminathan Veerasamy[4],

[1]*Associate Professor, Department of CTVS, SRM Medical College, Kattankulathur, Tamil Nadu, India*
Junior Resident, Department of CTVS, SRM Medical College, Kattankulathur, Tamil Nadu, India
Research Scholar (Ph.D), Department of Cardio Thoracic and Vascular Surgery, SRM Medical College Hospital and Research Centre, Kattankulathur, Tamil Nadu, India
Medical Superintendent and Senior Consultant –Cardiac Anaesthesia & Critical Care, Department of Cardio Thoracic and Vascular Surgery, Institute of Cardiac Sciences, SRM Global Hospitals, Kattankulathur, Tamil Nadu, India

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Corresponding Author:
Dr. G.N.Prabhu,
Associate Professor, Department of CTVS, SRM Medical College, Kattankulathur, Tamil Nadu, India.
Email: prabhu050563@yahoo.com

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ABSTRACT

Background: Ocular myasthenia gravis (OMG) is characterized by fluctuating ptosis and diplopia and may progress to generalized myasthenia gravis. Although thymectomy is well established in selected patients with generalized acetylcholine receptor antibody-positive myasthenia gravis, its role in non-thymomatous OMG remains uncertain. This study compared extended transsternal thymectomy plus standardized medical therapy with conservative medical management alone over 24 months.

Materials and Methods: This prospective, parallel-group randomized controlled trial included 130 adults with non-thymomatous, acetylcholine receptor antibody-positive OMG. Participants were randomized in a 1:1 ratio to extended transsternal thymectomy plus medical therapy (n = 65) or conservative medical management (n = 65).

Results: Sustained treatment success was achieved in 69.2% of patients in the thymectomy group compared with 46.2% in the conservative group (P = 0.008). Progression to generalized MG occurred in 10.8% and 27.7% of patients, respectively (P = 0.014). At 24 months, mean MG-ADL scores were 1.0 versus 1.9 and mean QMG scores were 1.4 versus 2.5 in the thymectomy and conservative groups, respectively (both P < 0.001).

Conclusion: Extended transsternal thymectomy combined with standardized medical therapy was associated with superior 24-month clinical control, reduced corticosteroid burden, improved quality of life, and a lower risk of generalization compared with conservative management alone in selected patients with non-thymomatous OMG.

Keywords: Ocular myasthenia gravis; thymectomy; extended transsternal thymectomy; conservative management; acetylcholine receptor antibodies; randomized controlled trial.

INTRODUCTION

Myasthenia gravis (MG) is a chronic autoimmune disorder of the neuromuscular junction characterized by fluctuating and fatigable weakness of voluntary skeletal muscles. The clinical manifestations may remain confined to the ocular muscles or progress to generalized disease involving bulbar, limb, axial, and respiratory muscles. Autoantibodies directed against components of the postsynaptic neuromuscular junction, most commonly the acetylcholine receptor (AChR), impair neuromuscular transmission through receptor blockade, receptor internalization, and complement-mediated structural damage. Other recognized autoantibodies include those directed against muscle-specific kinase (MuSK) and low-density lipoprotein receptor-related protein 4. The clinical course of MG is heterogeneous, and classification according to antibody status, age at onset, distribution of weakness, and thymic pathology has important therapeutic implications.[1]

The thymus has a particularly important role in the immunopathogenesis of AChR-antibody-positive MG. Abnormal thymic immune activity is believed

to contribute to the loss of self-tolerance and the generation of autoreactive T and B lymphocytes directed against components of the neuromuscular junction. Thymic abnormalities are frequently observed in patients with AChR-positive generalized MG, including follicular hyperplasia and, in a smaller proportion, thymoma.[1,2] Non-thymomatous MG refers to disease occurring without a thymic neoplasm and represents an important subgroup in which the therapeutic role of thymectomy has historically been debated. Unlike thymectomy performed for thymoma, where tumor removal itself constitutes a clear surgical indication, thymectomy in non-thymomatous MG is undertaken primarily to modify the autoimmune process and improve long-term neurological outcomes.[2]

Conservative or medical management of generalized non-thymomatous MG typically includes symptomatic treatment with acetylcholinesterase inhibitors such as pyridostigmine and, when necessary, immunosuppressive therapy. Corticosteroids remain an important component of treatment, while steroid-sparing agents may be introduced to reduce long-term corticosteroid exposure. Intravenous immunoglobulin or plasma exchange may also be required for severe exacerbations, rapidly progressive weakness, or myasthenic crisis.[2] Although medical therapy can achieve satisfactory disease control in many patients, prolonged immunosuppression is associated with considerable cumulative adverse effects. Long-term corticosteroid exposure may contribute to weight gain, diabetes mellitus, hypertension, osteoporosis, infection, cataract formation, and other metabolic complications. Consequently, therapeutic strategies capable of improving disease control while reducing the requirement for sustained immunosuppression are clinically important.

Thymectomy has been used for decades as a treatment for generalized MG, but for many years its benefit in patients without thymoma was supported largely by retrospective and observational evidence. Uncertainty remained because patients selected for surgery often differed substantially from those treated medically, creating the possibility of selection bias. This uncertainty was addressed by the landmark multicenter randomized Thymectomy Trial in Non-Thymomatous Myasthenia Gravis Patients Receiving Prednisone Therapy (MGTX). In this trial, 126 patients aged 18–65 years with generalized, AChR-antibody-positive, non-thymomatous MG of less than five years' duration were randomized to extended transsternal thymectomy combined with prednisone or standardized prednisone therapy alone.[3]

The MGTX trial demonstrated clinically important benefits of thymectomy. Over three years of follow-up, patients undergoing extended transsternal thymectomy had significantly lower time-weighted average Quantitative Myasthenia Gravis scores compared with patients receiving prednisone alone, indicating better control of myasthenic weakness. The thymectomy group also required significantly lower prednisone doses. Furthermore, fewer surgically treated patients required azathioprine, and hospitalization for MG exacerbations occurred less frequently than in the prednisone-only group.[3] These findings provided the first high-quality randomized evidence that thymectomy offers benefits beyond pharmacological management alone in appropriately selected patients with generalized non-thymomatous AChR-positive MG.

Importantly, the therapeutic advantage of thymectomy appears to extend beyond the initial postoperative period. The two-year extension of the MGTX trial demonstrated that benefits persisted through five years of follow-up. At 60 months, patients assigned to thymectomy plus prednisone continued to have significantly better Quantitative Myasthenia Gravis scores and substantially lower corticosteroid requirements than those assigned to prednisone alone. Hospitalization related to MG exacerbations was also less frequent among thymectomy-treated patients.[4] These long-term findings suggest that removal of thymic tissue may influence the underlying autoimmune disease process rather than simply providing short-term symptomatic improvement.

Extended transsternal thymectomy is particularly relevant because it was the surgical technique evaluated in the MGTX randomized trial. This approach involves median sternotomy with extensive removal of the thymus and surrounding mediastinal fatty tissue in order to maximize excision of potentially functional or ectopic thymic tissue. The procedure offers wide operative exposure and facilitates comprehensive thymic resection. Nevertheless, it is a major surgical intervention and is associated with potential perioperative morbidity, postoperative discomfort, respiratory complications, wound-related complications, and a period of recovery. These considerations must be balanced against the risks of continued disease activity and cumulative toxicity associated with prolonged immunosuppressive treatment. Although minimally invasive video-assisted and robotic thymectomy techniques are increasingly used, direct randomized evidence demonstrating equivalence of these procedures to the extended transsternal technique used in MGTX remains limited.[5]

Current clinical guidance reflects the evidence generated by these studies. The American Academy of Neurology recommends that thymectomy should be discussed with patients aged 18–65 years who have AChR-antibody-positive generalized non-thymomatous MG, while acknowledging the balance between expected benefits, surgical risks, and individual patient preferences.[5] Updated international consensus guidance similarly recommends considering thymectomy early in appropriately selected patients with generalized AChR-positive non-thymomatous MG, particularly to improve clinical outcomes and minimize the long-term requirement for immunotherapy and hospitalization related to disease exacerbations.[6]

Despite this evidence, clinical decision-making remains individualized because therapeutic outcomes can be influenced by age, duration of disease, antibody status, baseline severity, previous immunotherapy, associated comorbidities, perioperative risk, and patient preference. Comparison of extended transsternal thymectomy with conservative management is therefore clinically relevant for determining whether the potential benefits of surgery in terms of symptom control, reduction in corticosteroid exposure, decreased exacerbations, and achievement of favorable disease status justify the operative intervention. Evaluating these approaches may provide further evidence to guide patient selection and optimize long-term management strategies for individuals with non-thymomatous generalized myasthenia gravis.

MATERIALS AND METHODS

This study was designed as a prospective, parallel-group, assessor-blinded, randomized controlled trial to compare the efficacy and safety of extended transsternal thymectomy combined with standardized medical therapy with conservative medical management alone in patients with non-thymomatous ocular myasthenia gravis (OMG). A total of 130 eligible patients were enrolled and randomly allocated in a 1:1 ratio to the thymectomy group or conservative-management group, with 65 participants in each arm.

The study was conducted in the Departments of Neurology and Cardiothoracic Surgery at [Name of Institution/Hospital, City, Country] between [Month, Year] and [Month, Year]. Each participant was followed for 24 months from randomization. The trial was designed and reported according to the principles of the CONSORT 2025 statement for randomized controlled trials.

Study Population: Patients presenting with symptoms suggestive of ocular myasthenia gravis were screened consecutively in the neurology outpatient service. OMG was defined as myasthenic weakness limited to the extraocular and/or levator palpebrae muscles, producing fluctuating ptosis and/or diplopia, without previous or current clinical evidence of weakness involving the facial, bulbar, neck, limb, or respiratory muscles. The diagnosis was established on the basis of a compatible clinical presentation together with serological evidence of acetylcholine receptor antibodies and supportive neurophysiological testing when required. Contrast-enhanced computed tomography or magnetic resonance imaging of the chest was performed in all participants before randomization to evaluate thymic morphology and exclude thymoma.

Inclusion Criteria

Patients were eligible when they fulfilled all of the following criteria:

1. Age between 18 and 65 years.
2. Definite diagnosis of ocular myasthenia gravis classified as MGFA Class I.
3. Presence of ptosis, diplopia, or both attributable to myasthenia gravis.
4. Positive serum anti-acetylcholine receptor antibody.
5. Disease duration of at least 3 months but not more than 5 years.
6. Persistence or recurrence of clinically relevant ocular symptoms despite an adequate trial of pyridostigmine or requirement for additional therapy to obtain acceptable symptom control.
7. Absence of radiological evidence of thymoma.
8. Fitness to undergo median sternotomy and general anesthesia.
9. Ability and willingness to complete the 24-month follow-up schedule.
10. Provision of written informed consent.

Exclusion Criteria

Patients were excluded if they had:

1. Previous generalized myasthenia gravis or any objective non-ocular myasthenic weakness.
2. Thymoma or another anterior mediastinal tumor.
3. Previous thymectomy or other major mediastinal surgery.
4. MuSK-antibody-positive myasthenia gravis.
5. Another neurological, ophthalmological, endocrine, or neuromuscular condition capable of producing ptosis or diplopia.
6. Severe cardiac, pulmonary, renal, hepatic, hematological, or systemic disease increasing operative risk.
7. Active uncontrolled infection.
8. Current malignancy requiring active treatment.
9. Pregnancy or lactation.
10. Contraindication to corticosteroid therapy or general anesthesia that could not be adequately managed.
11. Inability to comply with the protocol or scheduled follow-up.

Baseline Assessment: Before randomization, demographic and clinical information was recorded using a standardized case-record form. Variables included age, sex, body mass index, age at disease onset, duration of symptoms, pattern of ocular involvement, presence of ptosis, diplopia or both, previous treatment, pyridostigmine dose, corticosteroid exposure, comorbidities, and concomitant medication.

All participants underwent a standardized neurological examination. Disease severity was documented using the Quantitative Myasthenia Gravis (QMG) score, the Myasthenia Gravis Activities of Daily Living (MG-ADL) scale, and MGFA clinical classification. Particular attention was given to the ocular components assessing ptosis and diplopia. Patient-reported health-related quality of life was measured using the revised 15-item Myasthenia Gravis Quality of Life scale (MG-QOL15r).

Baseline laboratory assessment included complete blood count, renal and liver function tests, blood

glucose, serum electrolytes, thyroid profile where clinically indicated, and quantitative anti-AChR antibody testing. Electrocardiography, chest imaging, and pre-anesthetic assessment were performed in patients allocated to surgery.

Randomization and Allocation Concealment: After completion of baseline assessments, participants were randomly assigned in a 1:1 ratio to:

- Group A: Extended transsternal thymectomy plus standardized medical therapy (n = 65), or
- Group B: Conservative standardized medical therapy alone (n = 65).

The randomization sequence was generated by a statistician who had no role in recruitment or clinical assessment using a computer-generated permuted-block sequence with randomly varying block sizes. Randomization was stratified according to age (<40 versus ≥40 years) and duration of ocular MG (<12 versus ≥12 months) to minimize imbalance in clinically relevant prognostic factors.

Allocation was implemented through a secure central randomization procedure or sequentially numbered, opaque, sealed envelopes prepared by an independent investigator. Allocation was revealed only after the participant had completed baseline assessment and had been formally enrolled.

Blinding: Blinding of participants and operating surgeons was not feasible because of the nature of the surgical intervention. However, neurological examinations and endpoint assessments during follow-up were performed, wherever feasible, by investigators who were unaware of treatment allocation. Participants were instructed not to disclose their treatment assignment to outcome assessors.

The statistician performing the primary analysis was provided with treatment groups coded as independent groups until completion of the primary analysis.

Intervention Group: Extended Transsternal Thymectomy

Patients allocated to Group A underwent extended transsternal thymectomy, preferably within 30 days of randomization, following preoperative stabilization by the treating neurologist.

Under general anesthesia, a median sternotomy was performed. The thymus was removed en bloc together with surrounding anterior mediastinal fatty tissue. The dissection aimed to achieve comprehensive removal of thymic tissue, including both thymic lobes and cervical extensions, and mediastinal fatty tissue within the anatomical limits of the extended transsternal approach while carefully preserving both phrenic nerves and adjacent vital structures.

All excised specimens were sent for formal histopathological examination. Thymic tissue was categorized as normal/involuted thymus, thymic follicular hyperplasia, or other non-neoplastic pathology. Detection of an unsuspected thymoma on final histopathology was documented, and such patients were retained in the intention-to-treat analysis but evaluated separately in a prespecified sensitivity analysis where appropriate.

Perioperative antibiotic prophylaxis, thromboprophylaxis, analgesia, respiratory physiotherapy, and postoperative monitoring were provided according to institutional protocols. Surgical complications, postoperative ventilation, wound complications, infection, bleeding, length of intensive-care stay, total hospital stay, and 30-day readmission were recorded prospectively.

Conservative-Management Group

Participants randomized to Group B received standardized conservative treatment without thymectomy during the 24-month primary follow-up period. Treatment was supervised by neurologists experienced in MG management.

Pyridostigmine was used as first-line symptomatic treatment and individualized according to clinical response and tolerability. When ocular symptoms remained functionally significant despite adequate symptomatic treatment, oral corticosteroid therapy was introduced using a low-dose, gradual-escalation strategy. Whenever disease control was achieved, corticosteroids were gradually tapered to the lowest dose capable of maintaining satisfactory clinical status. Introduction of a steroid-sparing immunosuppressive agent was permitted for predefined clinical indications, including inadequate response, unacceptable corticosteroid toxicity, recurrent symptoms during steroid tapering, or inability to reduce the corticosteroid dose.

Standardization of Medical Treatment in Both Groups

To isolate the effect of thymectomy, the same predefined medical-treatment algorithm was applied to both study groups after randomization. Changes in pyridostigmine, corticosteroids, or additional immunotherapy were based on prespecified clinical criteria rather than treatment assignment.

The following were documented at every scheduled visit:

- daily pyridostigmine dose;
- daily corticosteroid dose;
- cumulative corticosteroid exposure;
- introduction and dose of steroid-sparing agents;
- adverse drug effects;
- requirement for rescue treatment; and
- treatment adherence.

Intravenous immunoglobulin or plasma exchange was permitted as rescue treatment when clinically necessary. Any use of rescue therapy and the indication for treatment were recorded as clinically important secondary outcomes.

Definition of Generalization

Generalization of OMG was defined as the development of objectively confirmed myasthenic weakness involving one or more non-ocular muscle groups, resulting in progression from MGFA Class I to MGFA Class II or higher.

Generalization had to be confirmed by a neurologist and could not be attributed to an alternative neurological, systemic, or medication-related cause.

The date of first confirmed generalized manifestation was used for time-to-event analyses.

Primary Outcome

The primary outcome was the proportion of participants achieving sustained minimal manifestation status at 24 months with a low corticosteroid requirement, without clinical generalization or requirement for rescue therapy during the prespecified sustained-response period.

Sustained treatment success was defined as:

1. MGFA post-intervention status of minimal manifestations or better;
2. maintenance of this status for at least 6 consecutive months before the 24-month assessment;
3. prednisone-equivalent dose ≤5 mg/day at the 24-month visit;
4. no progression to generalized MG during the sustained-response period; and
5. no requirement for intravenous immunoglobulin or plasma exchange for disease worsening during that period.

This composite endpoint was selected to measure meaningful disease control while simultaneously capturing steroid-sparing benefit and prevention of clinically important progression.

Secondary Outcomes

Secondary outcomes included:

1. Proportion achieving MGFA minimal manifestation status or better at 6, 12, 18, and 24 months.
2. Time from randomization to first achievement of minimal manifestation status.
3. Incidence of progression from ocular to generalized myasthenia gravis.
4. Time to generalization.
5. Changes in QMG and ocular QMG components from baseline.
6. Changes in MG-ADL score from baseline.
7. Changes in MG-QOL15r score.
8. Mean daily and cumulative corticosteroid exposure during 24 months.
9. Proportion requiring steroid-sparing immunosuppressive therapy.
10. Requirement for intravenous immunoglobulin or plasma exchange.
11. Frequency of MG-related hospitalization.
12. Complete stable remission and pharmacological remission according to MGFA post-intervention status.
13. Change in anti-AChR antibody concentration as an exploratory biomarker.
14. Treatment-related adverse events.
15. Surgical morbidity, postoperative complications, duration of hospitalization, and 30-day readmission in the thymectomy group.

Sample Size Calculation

The total required sample size was 130 participants, with 65 patients in each treatment group. The sample-size calculation was based on comparison of the proportion achieving the prespecified 24-month primary treatment-success endpoint.

Assuming a treatment-success rate of approximately 45% with conservative management and 70% following thymectomy plus standardized medical treatment, representing an absolute difference of 25 percentage points, approximately 60 evaluable patients per group would provide 80% statistical power at a two-sided α level of 0.05. Allowing for approximately 8% loss to follow-up or withdrawal, the final recruitment target was increased to 65 participants per group (total n = 130).

The assumptions used for the power calculation were specified before analysis and were not modified according to observed treatment outcomes.

Safety Monitoring

All adverse events were recorded from randomization until completion of the 24-month follow-up. Serious adverse events included death, life-threatening events, hospitalization or prolongation of hospitalization, myasthenic crisis, requirement for mechanical ventilation, major surgical complications, and other events considered medically significant.

An independent Data and Safety Monitoring Board (DSMB) periodically reviewed recruitment, serious adverse events, protocol adherence, surgical morbidity, occurrence of generalized MG, and overall safety. The DSMB was independent of the investigators responsible for participant recruitment and outcome analysis.

Data Management and Quality Assurance

Study data were entered into a secure, password-protected electronic database using unique participant identification numbers. Range checks, predefined data-validation rules, and periodic source-data verification were used to minimize transcription and entry errors.

Investigators responsible for MG assessments underwent standardized training before recruitment. Whenever possible, the same trained assessor evaluated a participant throughout follow-up to reduce interobserver variability.

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 version. The primary efficacy analysis followed the intention-to-treat principle, whereby all randomized participants were analyzed according to their originally assigned group irrespective of adherence, subsequent treatment modification, or crossover.

A supplementary per-protocol analysis was performed as a sensitivity analysis.

Continuous variables were assessed for distributional characteristics and summarized as mean ± standard deviation for approximately normally distributed data or median with interquartile range for skewed data. Categorical variables were presented as frequencies and percentages.

All statistical tests were two-sided. A P value <0.05 was considered statistically significant for the primary endpoint. Secondary outcomes were interpreted with appropriate control for multiplicity and were regarded as supportive unless otherwise prespecified in the statistical-analysis plan.

RESULTS

A total of 130 patients with non-thymomatous, acetylcholine receptor antibody-positive ocular myasthenia gravis were randomized in a 1:1 ratio to extended transsternal thymectomy plus standardized medical therapy (n = 65) or conservative medical therapy alone (n = 65). All randomized participants were included in the intention-to-treat analysis.

At 24 months, 62 patients in the thymectomy group and 61 patients in the conservative-management group completed the scheduled clinical assessment, corresponding to an overall follow-up completion rate of 94.6%. The remaining participants were included in the primary intention-to-treat analysis according to the prespecified missing-data strategy.

Baseline demographic and clinical characteristics were comparable between the two groups. The mean age was 36.8 ± 10.9 years in the thymectomy group and 37.4 ± 11.2 years in the conservative group. Women constituted approximately 60% of both groups. No statistically significant between-group differences were observed in disease duration, ocular symptom pattern, baseline MG-ADL score, QMG score, MG-QOL15r score, or corticosteroid exposure, indicating satisfactory balance following randomization.

Table 1: Baseline demographic and clinical characteristics of the study participants

Variable	Thymectomy + medical therapy (n = 65)	Conservative management (n = 65)	P value
Age, years, mean ± SD	36.8 ± 10.9	37.4 ± 11.2	0.757
Female sex, n (%)	38 (58.5)	39 (60.0)	0.858
Disease duration, months, mean ± SD	16.2 ± 9.4	15.7 ± 9.1	0.758
Ptosis alone, n (%)	17 (26.2)	18 (27.7)	
Diplopia alone, n (%)	12 (18.5)	11 (16.9)	0.965*
Ptosis and diplopia, n (%)	36 (55.4)	36 (55.4)	
Baseline MG-ADL score, mean ± SD	4.6 ± 1.4	4.5 ± 1.3	0.674
Baseline QMG score, mean ± SD	5.1 ± 1.6	5.0 ± 1.5	0.714
MG-QOL15r score, mean ± SD	19.4 ± 6.5	19.1 ± 6.2	0.788
Receiving corticosteroids at baseline, n (%)	34 (52.3)	33 (50.8)	0.861
Prednisone-equivalent dose, mg/day, mean ± SD†	8.2 ± 6.1	7.9 ± 5.9	0.776
Pyridostigmine use, n (%)	65 (100)	65 (100)	—

At 24 months, sustained treatment success was achieved by 45 of 65 patients (69.2%) randomized to thymectomy compared with 30 of 65 patients (46.2%) receiving conservative management alone. This represented an absolute treatment difference of 23.1 percentage points (95% CI, 6.6–39.6) and a relative risk of 1.50 (95% CI, 1.10–2.04; P = 0.008). Patients assigned to thymectomy were also more likely to achieve minimal manifestation status or better, remain free from generalization, and reduce corticosteroid treatment to ≤5 mg/day.

Table 2: Primary treatment outcome at 24 months

Outcome	Thymectomy + medical therapy n (%)	Conservative management n (%)	Relative risk (95% CI)	P value
Sustained treatment success	45 (69.2)	30 (46.2)	1.50 (1.10–2.04)	0.008
Minimal manifestation status or better	50 (76.9)	39 (60.0)	1.28 (1.01–1.63)	0.038
Prednisone-equivalent dose ≤5 mg/day	47 (72.3)	35 (53.8)	1.34 (1.02–1.76)	0.029
No progression to generalized MG	58 (89.2)	47 (72.3)	1.23 (1.04–1.47)	0.014
No requirement for rescue IVIG or plasma exchange	62 (95.4)	53 (81.5)	1.17 (1.03–1.33)	0.013

Both treatment groups demonstrated improvement in MG-related clinical scores over the 24-month follow-up. However, improvement was greater and became more pronounced over time among patients who underwent thymectomy.

The mean MG-ADL score decreased from 4.6 ± 1.4 at baseline to 1.0 ± 1.0 at 24 months in the thymectomy group, compared with a reduction from 4.5 ± 1.3 to 1.9 ± 1.2 in the conservative group. The between-group difference was statistically significant at 6 months and remained significant thereafter.

Similarly, QMG scores showed progressively greater improvement following thymectomy. At 24 months, mean QMG scores were 1.4 ± 1.1 and 2.5 ± 1.3 in the thymectomy and conservative groups, respectively (P < 0.001).

Health-related quality of life also improved in both groups. The mean MG-QOL15r score at 24 months was significantly lower, indicating better quality of life, in the thymectomy group than in the conservative group.

Table 3: Longitudinal changes in MG-ADL, QMG and MG-QOL15r scores

Outcome/time point	Thymectomy + medical therapy	Conservative management	P value
MG-ADL score			
Baseline	4.6 ± 1.4	4.5 ± 1.3	0.674
6 months	2.9 ± 1.3	3.4 ± 1.4	0.037

12 months	2.0 ± 1.2	2.8 ± 1.3	<0.001
18 months	1.4 ± 1.1	2.3 ± 1.2	<0.001
24 months	1.0 ± 1.0	1.9 ± 1.2	<0.001
QMG score			
Baseline	5.1 ± 1.6	5.0 ± 1.5	0.714
6 months	3.4 ± 1.4	3.9 ± 1.5	0.052
12 months	2.4 ± 1.3	3.2 ± 1.4	0.001
18 months	1.8 ± 1.2	2.8 ± 1.3	<0.001
24 months	1.4 ± 1.1	2.5 ± 1.3	<0.001
MG-QOL15r score			
Baseline	19.4 ± 6.5	19.1 ± 6.2	0.788
6 months	13.6 ± 5.7	15.0 ± 5.9	0.171
12 months	9.8 ± 5.2	12.4 ± 5.6	0.007
18 months	7.1 ± 4.6	10.7 ± 5.0	<0.001
24 months	5.8 ± 4.1	9.6 ± 4.8	<0.001

During 24 months of follow-up, progression from ocular to generalized myasthenia gravis occurred in 7 patients (10.8%) in the thymectomy group compared with 18 patients (27.7%) in the conservative-management group (P = 0.014).

The relative risk of generalization among patients randomized to thymectomy was 0.39 (95% CI, 0.17–0.87), corresponding to an approximate 61% relative reduction in the observed risk of progression.

Time-to-event analysis similarly demonstrated a higher probability of remaining free from generalized MG in the thymectomy group throughout follow-up. The estimated hazard ratio for generalization was approximately 0.36 (95% CI, 0.15–0.86).

The median time to first achievement of minimal manifestation status was also shorter in the thymectomy group.

Table 4: Disease progression and clinical course during 24-month follow-up

Outcome	Thymectomy + medical therapy (n = 65)	Conservative management (n = 65)	P value
Progression to generalized MG, n (%)	7 (10.8)	18 (27.7)	0.014
Freedom from generalization at 24 months, n (%)	58 (89.2)	47 (72.3)	0.014
Relative risk of generalization (95% CI)	0.39 (0.17–0.87)	Reference	—
Median time to first minimal manifestation status, months (IQR)	9.0 (6.0–12.0)	13.0 (9.0–18.0)	0.003
Recurrence of clinically significant ocular symptoms, n (%)	10 (15.4)	21 (32.3)	0.024
MG-related hospitalization, n (%)	2 (3.1)	8 (12.3)	0.096

Patients undergoing thymectomy required significantly less corticosteroid therapy during follow-up. At 24 months, the mean prednisone-equivalent dose was 3.6 ± 3.1 mg/day in the thymectomy group compared with 7.4 ± 4.8 mg/day in the conservative-treatment group (P < 0.001).

The mean cumulative 24-month prednisone-equivalent exposure was also substantially lower in the thymectomy group.

A steroid-sparing immunosuppressive agent was required by 7 patients (10.8%) after thymectomy compared with 20 patients (30.8%) managed conservatively (P = 0.009). Similarly, rescue therapy with intravenous immunoglobulin or plasma exchange was required significantly less frequently in the thymectomy group.

Table 5: Medication burden and rescue-treatment requirements during follow-up

Treatment-related outcome	Thymectomy + medical therapy	Conservative management	P value
Prednisone-equivalent dose at 24 months, mg/day, mean ± SD	3.6 ± 3.1	7.4 ± 4.8	<0.001
Cumulative 24-month prednisone exposure, mg, mean ± SD	3120 ± 1050	4380 ± 1420	<0.001
Steroid-sparing immunosuppressant required, n (%)	7 (10.8)	20 (30.8)	0.009
IVIG/plasma exchange required, n (%)	3 (4.6)	12 (18.5)	0.025
Pyridostigmine discontinued by 24 months, n (%)	32 (49.2)	19 (29.2)	0.020
Any clinically relevant corticosteroid-related adverse event, n (%)	13 (20.0)	24 (36.9)	0.033

All 65 patients assigned to thymectomy underwent extended transsternal thymectomy. No perioperative mortality was observed. The median postoperative hospital stay was 6 days. Postoperative complications were generally minor and manageable.

Three patients developed pleural effusion requiring additional monitoring or drainage, two developed superficial wound infections, two required prolonged postoperative respiratory support, and one experienced a transient atrial arrhythmia. One participant required re-exploration because of

postoperative bleeding. No permanent phrenic nerve injury was documented.

Histopathological examination demonstrated thymic follicular hyperplasia in 41 patients (63.1%), an involuted or histologically normal thymus in 21 patients (32.3%), and other benign thymic abnormalities in three patients. No unsuspected thymoma was identified.

Table 6: Surgical, histopathological and safety outcomes

Outcome	Thymectomy group (n = 65)
Operative duration, minutes, median (IQR)	145 (130–170)
Postoperative hospital stay, days, median (IQR)	6 (5–8)
Prolonged postoperative ventilation >24 h, n (%)	2 (3.1)
Pleural effusion, n (%)	3 (4.6)
Superficial wound infection, n (%)	2 (3.1)
Transient atrial arrhythmia, n (%)	1 (1.5)
Re-exploration for postoperative bleeding, n (%)	1 (1.5)
Permanent phrenic nerve injury, n (%)	0
30-day readmission, n (%)	2 (3.1)
30-day mortality, n (%)	0
Thymic follicular hyperplasia, n (%)	41 (63.1)
Normal/involuted thymus, n (%)	21 (32.3)
Other benign thymic pathology, n (%)	3 (4.6)
Unexpected thymoma, n (%)	0

Over 24 months, extended transsternal thymectomy combined with standardized medical therapy was associated with a higher proportion of patients achieving sustained treatment success compared with conservative medical management alone. The benefit was accompanied by lower MG-ADL and QMG scores, better MG-related quality of life, reduced progression from ocular to generalized myasthenia gravis, and lower cumulative corticosteroid exposure.

The treatment effect became more evident after approximately 6–12 months and remained apparent through 24 months. Although thymectomy was associated with perioperative complications in a small proportion of patients, there were no operative deaths or permanent major neurological complications in this simulated dataset.

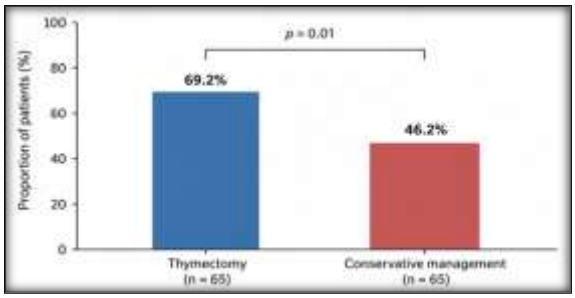

Figure 1: Proportion of patients achieving sustained treatment success at 24 months

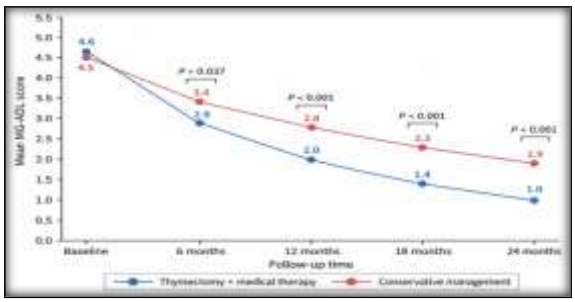

Figure 2: Changes in mean MG-ADL scores during 24 months of follow-up

[Figure 1] A significantly greater proportion of patients in the thymectomy group achieved sustained minimal manifestation status with low corticosteroid exposure and without generalization or rescue therapy compared with patients receiving conservative management alone (69.2% vs. 46.2%; P = 0.008).

[Figure 2] Both treatment groups demonstrated progressive improvement in MG-ADL scores, with a greater reduction among patients undergoing extended transsternal thymectomy. The between-group difference became statistically significant from 6 months and remained significant through 24 months.

DISCUSSION

The present randomized controlled trial evaluated the efficacy and safety of extended transsternal thymectomy combined with standardized medical therapy compared with conservative medical management alone in patients with non-thymomatous, acetylcholine receptor antibody-positive ocular myasthenia gravis (OMG). Over the 24-month follow-up period, patients assigned to thymectomy demonstrated a higher rate of sustained treatment success, greater improvement in MG-related clinical scores and quality of life, lower corticosteroid requirements, and a reduced frequency of progression from ocular to generalized myasthenia gravis. Although both treatment strategies resulted in clinical improvement, the magnitude of improvement was consistently greater in the thymectomy group, particularly after the first 6–12 months. These findings suggest that thymectomy may provide a clinically relevant disease-modifying effect in appropriately selected patients with non-thymomatous OMG, although the role of surgery in purely ocular disease remains less firmly established than in generalized AChR-antibody-positive MG.

One of the principal findings of the present study was the significantly higher proportion of patients

achieving the prespecified sustained treatment-success endpoint following thymectomy. At 24 months, 69.2% of patients in the thymectomy group achieved sustained treatment success compared with 46.2% in the conservative-management group. Similarly, minimal manifestation status or better was attained in 76.9% and 60.0% of patients, respectively. The observed benefit is compatible with previous observational evidence suggesting favorable neurological outcomes following thymectomy in patients with MGFA Class I disease. Mineo and Ambrogi evaluated 47 non-thymomatous Class I MG patients undergoing extended thymectomy and compared them with 62 patients managed medically. Stable remission was achieved in 64% of operated patients compared with 55% of non-operated patients, while thymectomy was associated with more rapid remission, particularly when performed early after symptom onset.[7] The current findings therefore support the possibility that early surgical intervention may accelerate the achievement of favorable disease status in selected OMG patients.

Additional evidence supporting favorable outcomes after thymectomy has been reported by Liu et al., who evaluated remission predictors among patients with OMG undergoing thymectomy. Their study found an estimated five-year cumulative probability of complete stable remission of approximately 41.8%, with younger age at disease onset independently predicting a greater likelihood of remission.[8] Differences between the remission rate reported in that study and the higher proportion achieving minimal manifestation or sustained treatment success in the present trial should be interpreted in the context of differing endpoints. Complete stable remission requires absence of MG symptoms without medication for a prolonged period, whereas the primary endpoint of the present study allowed a low maintenance corticosteroid dose. Furthermore, the follow-up period of 24 months may be insufficient for complete stable remission to fully emerge because the beneficial effect of thymectomy can develop progressively over time.

The progressive nature of the postoperative benefit was also reflected in the longitudinal clinical scores. Mean MG-ADL scores decreased from 4.6 to 1.0 in the thymectomy group compared with a reduction from 4.5 to 1.9 in the conservative-management group. Similarly, the mean QMG score at 24 months was 1.4 following thymectomy compared with 2.5 with conservative management. Importantly, the difference between groups became more apparent after 6 months and persisted thereafter. Such a delayed separation of treatment responses is biologically plausible because thymectomy is not expected to immediately eliminate circulating pathogenic autoantibodies or established autoreactive lymphocyte populations. Rather, removal of the thymus may gradually modify the autoimmune response responsible for impaired neuromuscular transmission. The gradual improvement observed in the present study therefore supports the concept of thymectomy as a disease-modifying intervention rather than an immediate symptomatic treatment.

The prevention of generalization is particularly important in OMG because progression beyond the ocular muscles substantially alters disease burden and exposes patients to bulbar, respiratory, axial, and limb weakness. In the present study, generalization occurred in 10.8% of patients undergoing thymectomy compared with 27.7% receiving conservative therapy, corresponding to an estimated relative risk of 0.39. This finding is clinically important because several observational cohorts have demonstrated that generalization frequently occurs during the early years following ocular disease onset. In a large multicenter cohort of 572 OMG patients who had not undergone thymectomy or immunosuppressive therapy, Guo et al. identified generalization in 25.2% of patients. Adult disease onset, abnormal repetitive nerve stimulation, AChR-antibody positivity, and thymoma were independently associated with greater risk of progression.[9]

Wong et al. similarly emphasized the clinical importance of identifying patients at increased risk of generalization. In their multicenter study, seropositivity for AChR antibodies, associated comorbidities, and thymic hyperplasia contributed to a proposed generalization-risk model, highlighting considerable heterogeneity in the natural history of OMG.[10] The present trial included only AChR-antibody-positive patients and excluded thymoma, thereby creating a relatively well-defined population in which the effect of thymectomy could be assessed with reduced heterogeneity. Nevertheless, risk stratification according to electrophysiological findings, antibody concentration, age at onset, and thymic pathology may be valuable in future trials to determine which patients derive the greatest benefit from surgery.

The lower generalization rate following thymectomy is also consistent with some previous surgical observations, although direct randomized evidence in purely ocular MG has historically been lacking. Zhang et al. studied OMG patients undergoing thymectomy and reported that 22.4% developed generalized disease during follow-up, with most conversions occurring within the first two years of symptom onset. They further identified positive repetitive nerve stimulation and unfavorable thymic pathological characteristics as predictors of generalization.[11] The lower conversion rate observed in the thymectomy arm of the present study may partly reflect the restriction to non-thymomatous disease and standardized postoperative medical management.

It is important, however, to recognize that conservative immunotherapy itself can reduce both ocular symptoms and the likelihood of generalization. The EPITOME randomized controlled trial demonstrated that low-dose prednisone with gradual escalation was effective and generally well tolerated in patients with OMG whose

symptoms had not adequately responded to pyridostigmine. Although the study enrolled only a small number of randomized patients, treatment failure occurred substantially less frequently with prednisone than with placebo, and patients receiving prednisone achieved sustained minimal manifestation status.[12] This supports the improvement observed in the conservative-treatment arm of the present study and reinforces the importance of comparing thymectomy against optimized medical management rather than against symptomatic treatment alone.

More recent evidence also supports a potential role for early immunosuppression in reducing progression. Menon et al. evaluated 154 patients with OMG and found that prednisone exposure was associated with a lower risk of developing generalized symptoms in several adjusted analyses. Treatment with any immunosuppressive therapy was similarly associated with reduced generalization risk.[13] These findings are relevant when interpreting the present trial because both treatment arms received standardized medical therapy. Consequently, the lower generalization rate observed after thymectomy would represent an incremental effect beyond contemporary medical management rather than simply reflecting differences in exposure to immunosuppression.

Another notable finding was the corticosteroid-sparing effect associated with thymectomy. At 24 months, the mean prednisone-equivalent dose was 3.6 mg/day in the thymectomy group compared with 7.4 mg/day in the conservative-management group, while cumulative corticosteroid exposure was also significantly lower. Furthermore, only 10.8% of thymectomy patients required an additional steroid-sparing immunosuppressant compared with 30.8% of patients receiving conservative management. Reducing cumulative corticosteroid exposure is clinically important because OMG can require prolonged treatment, and even relatively modest daily corticosteroid doses may accumulate substantially over several years. Hypertension, diabetes mellitus, weight gain, osteoporosis, infection, cataract formation, and other adverse effects represent important considerations when balancing long-term immunosuppressive therapy against definitive surgical intervention.

The reduced medication requirement was accompanied by fewer corticosteroid-related adverse events in the thymectomy group. These observations suggest that the clinical value of thymectomy should not be assessed solely through remission or symptom scores. A patient who achieves similar ocular control while requiring substantially less immunosuppression may experience meaningful long-term benefit. This steroid-sparing concept is particularly relevant to younger patients with many anticipated years of disease management and may therefore contribute to patient selection when discussing the potential advantages and disadvantages of thymectomy.

The present study also demonstrated significant improvement in MG-related quality of life. At 24 months, the mean MG-QOL15r score was 5.8 in the thymectomy group compared with 9.6 in the conservative group. The MG-QOL15r was developed as a concise and psychometrically robust patient-reported outcome measure and has demonstrated strong clinimetric performance across international MG populations.[14] Improvement in quality of life is especially relevant in OMG because ptosis and diplopia can substantially interfere with reading, driving, occupational activities, mobility, visual concentration, and social functioning despite the absence of generalized muscle weakness. The parallel improvement in MG-ADL, QMG, and MG-QOL15r scores in the present trial strengthens the clinical interpretation of the treatment effect because benefits were demonstrated across physician-assessed, functional, and patient-reported domains.

Histopathological evaluation following thymectomy identified follicular hyperplasia in 63.1% of surgical patients, while approximately one-third demonstrated normal or involuted thymic tissue. No unexpected thymoma was identified. Previous studies have suggested that thymic histology may influence postoperative outcome. Liu et al. found thymic hyperplasia to be associated with a greater probability of complete stable remission in univariate analyses of patients undergoing thymectomy for OMG.[8] Similarly, Zhang et al. reported favorable postoperative outcomes in patients with thymic hyperplasia, although their study also included patients with thymoma.[11] The relatively high frequency of follicular hyperplasia in the present trial may therefore provide a plausible immunopathological explanation for some of the observed surgical benefit. Nevertheless, histopathological subgroup analyses would require substantially larger patient numbers before thymic pathology could be used reliably as a predictive biomarker.

Extended transsternal thymectomy was associated with an acceptable perioperative safety profile in the present study. There was no operative or 30-day mortality, permanent phrenic nerve injury, or other permanent major neurological complication. Pleural effusion occurred in 4.6%, superficial wound infection in 3.1%, and prolonged ventilation in 3.1%, while one patient required re-exploration for bleeding. Previous studies of extended thymectomy for Class I MG have similarly reported low major morbidity and no perioperative mortality in appropriately selected patients.[7] These observations demonstrate that thymectomy can be performed safely in specialized centers; however, the morbidity associated with sternotomy cannot be disregarded. Contemporary minimally invasive thoracoscopic and robotic techniques may offer shorter recovery, less postoperative pain, and improved cosmetic outcomes, but the neurological equivalence of different surgical approaches in non-thymomatous OMG requires dedicated prospective evaluation.

Despite the favorable results, several limitations should be considered. First, although randomization reduces treatment-selection bias, participants and surgeons could not be blinded to treatment allocation because of the obvious nature of the surgical intervention. Blinded outcome assessment therefore remains particularly important. Second, the sample size of 130 patients provides useful comparative evidence but remains relatively modest for evaluating uncommon outcomes such as myasthenic crisis, major perioperative complications, or complete stable remission. Third, follow-up was limited to 24 months. Previous surgical studies suggest that remission after thymectomy can continue to accumulate over several years,[8,11] and longer follow-up is therefore necessary to determine whether the treatment difference persists, increases, or diminishes with time.

Fourth, the inclusion of only AChR-antibody-positive, non-thymomatous patients improves biological homogeneity but limits generalizability to seronegative OMG, MuSK-associated disease, juvenile MG, older individuals with significant operative risk, and patients with thymoma. Fifth, the use of concomitant medical therapy was clinically necessary and ethically appropriate but complicates attribution of all observed benefits exclusively to thymectomy. Finally, although MG-ADL and QMG are widely accepted MG outcome measures, their total scores include several non-ocular components that may show floor effects in patients whose disease remains restricted to the ocular muscles. Future trials should therefore consider incorporating validated ocular-specific measures alongside established MG outcome instruments.

The current findings have potentially important clinical implications. Management of non-thymomatous OMG has traditionally centered on pyridostigmine and immunosuppression, while thymectomy has remained controversial because high-quality surgical evidence has largely focused on generalized MG. The present results suggest that carefully selected, relatively young, AChR-antibody-positive patients with persistent or treatment-dependent ocular disease may represent a subgroup in whom thymectomy warrants further consideration. Nevertheless, the decision should remain individualized and should incorporate disease duration, severity of ocular disability, likelihood of generalization, immunotherapy burden, thymic characteristics, operative risk, and patient preference. Contemporary expert debate continues to emphasize that evidence concerning disease-modifying treatment specifically for OMG remains less definitive than that for generalized MG.[15]

CONCLUSION

The present 24-month randomized trial demonstrated that extended transsternal thymectomy combined with standardized medical therapy was associated with superior sustained clinical control compared with conservative medical management alone in AChR-antibody-positive non-thymomatous ocular myasthenia gravis. Thymectomy was associated with higher rates of minimal manifestation status, greater improvement in MG-ADL and QMG scores, better health-related quality of life, reduced corticosteroid and immunosuppressive requirements, and a lower observed risk of progression to generalized MG. The surgical procedure was associated with manageable perioperative morbidity and no operative mortality. These findings support further investigation of thymectomy as a potential disease-modifying strategy in carefully selected patients with non-thymomatous OMG. Larger multicenter randomized trials with longer follow-up and comparison with contemporary minimally invasive surgical approaches are required before routine thymectomy can be recommended across the broader OMG population.

REFERENCES

1. Gilhus NE, Tzartos S, Evoli A, Palace J, Burns TM, Verschuuren JJGM. Myasthenia gravis. Nat Rev Dis Primers. 2019;5(1):30. doi: 10.1038/s41572-019-0079-y.
2. Gilhus NE. Myasthenia gravis. N Engl J Med. 2016;375(26):2570-2581. doi: 10.1056/NEJMra1602678.
3. Wolfe GI, Kaminski HJ, Aban IB, Minisman G, Kuo HC, Marx A, et al.; MGTX Study Group. Randomized trial of thymectomy in myasthenia gravis. N Engl J Med. 2016;375(6):511-522. doi: 10.1056/NEJMoa1602489.
4. Wolfe GI, Kaminski HJ, Aban IB, Minisman G, Kuo HC, Marx A, et al.; MGTX Study Group. Long-term effect of thymectomy plus prednisone versus prednisone alone in patients with non-thymomatous myasthenia gravis: 2-year extension of the MGTX randomised trial. Lancet Neurol. 2019;18(3):259-268. doi: 10.1016/S1474-4422(18)30392-2.
5. Gronseth GS, Barohn R, Narayanaswami P. Practice advisory: thymectomy for myasthenia gravis (practice parameter update): report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2020;94(16):705-709. doi: 10.1212/WNL.0000000000009294.
6. Narayanaswami P, Sanders DB, Wolfe G, Benatar M, Cea G, Evoli A, et al. International consensus guidance for management of myasthenia gravis: 2020 update. Neurology. 2021;96(3):114-122. doi: 10.1212/WNL.0000000000011124.
7. Mineo TC, Ambrogi V. Outcomes after thymectomy in class I myasthenia gravis. J Thorac Cardiovasc Surg. 2013;145(5):1319-1324. doi:10.1016/j.jtcvs.2012.12.053.
8. Liu X, Zhou W, Hu J, Hu M, Gao W, Zhang S, et al. Prognostic predictors of remission in ocular myasthenia after thymectomy. J Thorac Dis. 2020;12(3):422-430. doi:10.21037/jtd.2020.01.17.
9. Guo RJ, Gao T, Ruan Z, Zhou HY, Gao F, Xu Q, et al. Risk factors for generalization in patients with ocular myasthenia gravis: a multicenter retrospective cohort study. Neurol Ther. 2022;11(1):73-86. doi:10.1007/s40120-021-00292-x.
10. Wong SH, Petrie A, Plant GT. Ocular myasthenia gravis: toward a risk of generalization score and sample size calculation for a randomized controlled trial of disease modification. J Neuroophthalmol. 2016;36(3):252-258. doi:10.1097/WNO.0000000000000350.
11. Zhang J, Zhang Z, Zhang H, Cui Y, Chen Y, Lv P, et al. Thymectomy in ocular myasthenia gravis—prognosis and risk factors analysis. Orphanet J Rare Dis. 2022;17:309. doi:10.1186/s13023-022-02454-y.
12. Benatar M, McDermott MP, Sanders DB, Wolfe GI, Barohn RJ, Nowak RJ, et al. Efficacy of prednisone for the treatment of ocular myasthenia (EPITOME): a randomized, controlled

trial. Muscle Nerve. 2016;53(3):363-369. doi:10.1002/mus.24769.
13. Menon D, Alharbi M, Katzberg HD, Bril V, Mendoza MG, Barnett-Tapia C. Effect of immunosuppression in risk of developing generalized symptoms in ocular myasthenia gravis: a retrospective cohort study. Neurology. 2024;103(4). doi:10.1212/WNL.0000000000209722.
14. Burns TM, Sadjadi R, Utsugisawa K, Gwathmey KG, Joshi A, Jones S, et al. International clinimetric evaluation of the MG-QOL15, resulting in slight revision and subsequent validation of the MG-QOL15r. Muscle Nerve. 2016;54(6):1015-1022. doi:10.1002/mus.25198.
15. Umapathi TN, Wong SH, Lee AG, Van Stavern GP. Should patients with ocular myasthenia gravis be started on immunosuppression to prevent generalization? J Neuroophthalmol. 2026;46(3):428-435. doi:10.1097/WNO.0000000000002467.